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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/805,785 | 03/13/2001 | Tony Baker | SDB-001CN | 2845 |

30623 7590 10/02/2002

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| EXAMINER | |
|---|---|
| SOUAYA, JEHANNE E | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 10/02/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/805,785 | Baker |
| **Examiner** | **Art Unit** |
| Jehanne Souaya | 1634 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Feb 26, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *15-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *15-24* is/are rejected.

7) ☒ Claim(s) *15 and 21* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

1. The preliminary amendment filed 2/25/2002 has been received and entered into the instant application. Consequently, claims 15-21 and newly added claims 22-24 are pending in the instant application and an action on the merits of claims 15-24 is set forth below. Claims 1-14 have been canceled.

### *Priority*

2. Applicants claim for priority to applications 09/185,402, filed 11/3/1998 and 08/988,029, filed 12/10/1997 is noted. The claims have been awarded benefit of the '402 filing date, however the subject matter of the claims was not disclosed in the '089 application, therefore the effective filing date of the instantly pending claims is that of 11/3/1998.

### *Claim Objections*

3. Claims 15 and 21 are objected to because of the following informalities: the claims include brackets, ie: [] in reciting the name of chemical compounds. Procedurally, the use of brackets "[]" in claims normally indicate deleted subject matter. Applicant should be advised that should the claims be found allowable, the use of these brackets could be mistaken to mean deleted subjected matter.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 lacks sufficient antecedent basis for the term "said nucleic acid" as the term "nucleic acid" does not appear in the claim or any claim from which claim 18 depends.

Claims 20 and 24 lack sufficient antecedent basis for the term "the polymerase chain reaction".

Claim 22 is indefinite as it cannot be determined which 'nucleic acid' is being referred to, the "nucleic acids" in the preamble of claim 21, the "test nucleic acid" or the "target nucleic acid".

### *Claim Rejections - 35 USC § 102*

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-

> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

7. Claims 15 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Chung et al (Mol Cells. Vol. 6, pp 108-111, 1996).

The claims are drawn to a method of improving the signal response of a molecular assay by adding a solution containing a divalent metal chelator in the range of from about 0.001M to 0.1M and a chelator enhancing component in the range of from about 0.1M to 2M to a test sample, extracting molecular analytes of interest from the sample, and conducting a molecular assay the extracted molecular analytes. Chung et al teach an improved method of isolating quality polysaccharide free RNA from plant tissues by 1) adding an extraction buffer (buffer A) comprising 300 mM (0.3M) LiCl and 10mM (0.01M) EDTA to a sample (test sample) of pulverized sesame and perilla oilseeds (see p. 109, col. 1, "Solutions", "Procedure"), 2) extracting RNA (extracting molecular analytes of interest) (p. 109, cols 1 and 2 "procedure"), and 3) spectrophotometrically and electrophoretically (p. 109, last para, table 1, Figure 1) assessing the quality and quantity of extracted RNA (conducting a molecular assay on the extracted molecular analytes of interest). Chung specifically teaches that the quality of RNA was dependent on the RNA extraction buffer used and that buffer A greatly enhanced the RNA

quality isolated from oilseeds of sesame and perilla (p. 110, col. 1, lines 1-4), thus buffer A used by Chung can be said to have 'preserved' the test sample. Table 1 of Chung teaches enhanced absorbance ratios (improved signal response) and Figure 1 of Chung teaches clearer bands on an agarose gel with the use of buffer A. Claim 20 is drawn to the method wherein the molecular assay is selected from PCR, ligase chain technology test, and a genetic transformation test. Chung teaches constructing cDNA libraries from RNA populations acquired using buffer A, and that northern hybridization using cDNA probes shoed that the RNA isolated was intact and functional (page 111- first para, figure 2 ), therefore Chung inherently teaches an RT-PCR method with improved signal (figure 2) (in this case, "signal response" is broadly interpreted to encompass intact and functional cDNA derived from isolated RNA using buffer A).

8. Claims 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Sigman et al (WO 93/03167, 2/18/1993).

Sigman teaches a method of isolating and preserving DNA. Sigman teaches that there is a need to isolate and prevent degradation of DNA in blood samples from patients suspected of infection with parasites, such as T. Cruzi (eukaryotic DNA) or other infectious agents during storage (p. 3, lines 16-19). Sigman teaches that isolation and storage comprise contacting a biological sample containing DNA in cells with a buffer (aqueous solution) containing a nonamphipathic chaotropic salt (chelator enhancing component) such as guanidine thiocyanate or guanidine chloride and a concentration of a chelating agent (divalent metal chelator) such as

EDTA (see p. 9, lines 1-11). Sigman teaches that the method is suitable for use on any biological sample including human blood, urine, sputum and lymphatic fluid (claims 16 and 17) (p. 12, lines 15-21). Sigman teaches that preferably, the guanidinium chloride is present in at least 3 molar concentration and the chelating agent in at least 0.1 molar concentration in the mixture of the biological sample and storage buffer (with regard to claim 15, Sigman teaches a solution that contains a divalent metal chelator in an amount of *at least* about 0.01M). Sigman specifically teaches that human intravenous blood was freshly drawn and added to a tube containing guanidinium chloride and EDTA so that the final concentration of each was 3M and .1M respectively (p. 26, Example 1). Sigman teaches that the DNA was extracted (extracting molecular analytes of interest) and electrophoresed (conducting a molecular assay) and that the DNA stored in a mixture of the buffer remains intact at 37 deg. C for at least a month (page 27 and Figure 1). As Sigman teaches that there is a need to prevent DNA degradation in blood samples (p. 3, lines 16-20), the method of Sigman inherently improves the signal response of the electrophoresis step taught by Sigman in example 1 as the intact DNA bands visible on the gel is an inherent improvement over the smear of DNA that would be observed should the DNA have been degraded. As Sigman specifically teaches that the DNA stored in the GnCl and EDTA buffer was intact for at least a month, the buffer used by Sigman inherently "preserves" the test sample (blood sample). With regard to claim 20, Sigman teaches that there is a need to prepare the DNA for amplification (p. 3, lines 20-21). Sigman specifically teaches a polymerase chain reaction on cleaved minicircle DNA extracted from a blood/GnCl/ EDTA (GEB lysate) sample

(see examples 3 and 4). Sigman teaches that using the GEB lysate, PCR amplification of extracted minicircles was sensitive enough that a single T.cruzi cell could be detected in 20 ml of blood (p. 35).

It is noted that the claims recite concentrations in a range of from about 0.001 to 0.1 molar for the chelator and a range from about 0.1M to 2M for the chelator enhancing component. With regard to the chelator enhancing component and the chelator, it is noted that the specification does not teach what concentrations this range encompasses. Further, since the difference between the high and low end of the range is 20 fold and the claims recite that the entire range (emphasis added) can be *about* 0.1M to 2M for the chelator enhancing component, it cannot be determined from the teachings in the specification or the recitation in the claims how far above the higher end or how far below the lower end of the range is encompassed by the claims. Therefore, the claims have been interpreted broadly to encompass a higher end of 3M for the chelator enhancing component.

9. Claims 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang (WO 95/35390; 12/28/1995).

The claims are drawn to a method comprising contacting a test nucleic acid with a solution comprising a divalent metal chelator in the range of from about 0.001M to 0.1M and a chelator enhancing component in the range of from about 0.1M to 2M to form a test solution and contacting the test solution with a target nucleic acid under conditions favorable for hybridization

such that hybridization occurs. It is noted that the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively.

Zhang teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA to an equal volume of sample (eg serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30), and subsequently adding nucleic acid amplification probes (target nucleic acid and claim 24) and paramagnetic beads to the solution containing lysis buffer and nucleic acids from the sample. Zhang specifically teaches that hybridization occurs between the nucleic acid from the sample and the probes (p.17, lines 19-20). Zhang specifically teaches that the method can be used for detection of genetic variations in samples from patients with genetic diseases or neoplasia (page 4, lines 13-23, page 5, lines 12-19- eukaryotic DNA).

It is noted that the preamble is drawn to "a method of improving hybridization of nucleic acids". However, the recitation of "improve hybridization of nucleic acids" does not carry patentable weight to overcome the teachings of Zhang as the positive process steps of the claimed method are taught by Zhang in the same order.

10. Claims 21-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Becker et al (US Patent 6.130,038, 102(e) date: 7/16/1996).

The claims are drawn to a method comprising contacting a test nucleic acid with a solution comprising a divalent metal chelator in the range of from about 0.001M to 0.1M and a

chelator enhancing component in the range of from about 0.1M to 2M to form a test solution and contacting the test solution with a target nucleic acid under conditions favorable for hybridization such that hybridization occurs. It is noted that the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively.

Becker specifically teaches that hybridization between nucleic acids is enhanced in a solution containing 1.0 M LiCl (see example 9, coll 32). Becker teaches a method of hybridization between 2'-O-methyl nucleotides and a complementary RNA molecule. Becker specifically teaches (it is noted that example 9 refers to reaction conditions as in example 6(d), col. 30, which in turn refers to reaction conditions as in example 1 "chemiluminescent method", col. 24) a method wherein RNA and oligonucleotide probes are allowed to hybridize in a buffer containing lithium chloride (example 9 is drawn to using LiCl instead of Lithium succinate) and 1.5 mM (.0015M) EDTA. It is noted that Becker does not specifically teach the order of steps that the different nucleic acids (RNA or oligonucleotide probes) were added to the buffer, however, the order of steps is not essential to the method. Becker inherently teaches that a first nucleic acid is added to the buffer (forming a "test solution") and then a second nucleic acid is added to the solution containing buffer and nucleic acid.

***Double Patenting***

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 15-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and 7-8 of U.S. Patent No. 6,458,546, view of Sigman et al (WO 93/03167, 2/18/1993).

Instant claims 15-20 are drawn to a method of improving the signal response of a molecular assay by adding a solution containing a divalent metal chelator in the range of from about 0.001M to 0.1M and a chelator enhancing component in the range of from about 0.1M to 2M to a test sample, which can be a biological fluid, extracting molecular analytes of interest

from the sample, and conducting a molecular assay on the extracted molecular analytes. Claims 1-5 and 7-8 of the '546 patent are drawn to preserving nucleic acids in a biological fluid by contacting the biological fluid with a solution containing a divalent metal chelator in the range of from about 0.001M to 0.1M and a chelator enhancing component in the range of from about 0.1M to 2M. Although the claims of the '546 patent do not disclose extracting the nucleic acids and conducting a molecular assay on the extracted nucleic acids, Sigman teaches a method of isolating and preserving DNA and extracting the isolated and preserved DNA to perform molecular assays, such as hybridization and PCR on the extracted DNA (p. 3, lines 16-19). Sigman specifically teaches that the DNA was extracted (extracting molecular analytes of interest) and electrophoresed (conducting a molecular assay) and T.cruzi nucleic acids were identified. With regard to claim 20, Sigman teaches that there is a need to prepare the DNA for amplification (p. 3, lines 20-21). Sigman specifically teaches a polymerase chain reaction on cleaved minicircle DNA extracted from a blood/GnCl/ EDTA (GEB lysate) sample (see examples 3 and 4). Sigman teaches that using the GEB lysate, PCR amplification of extracted minicircles was sensitive enough that a single T.cruzi cell could be detected in 20 ml of blood (p. 35). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to extract and assay the nucleic acids preserved in the claims of the '546 patent for the purpose of sequencing, or identifying the origin of the DNA preserved, for example to identify infective pathogens in a sample of blood from a patient as taught by Sigman. The ordinary artisan would have been motivated to extract and assay the nucleic acids preserved

in the method of the '546 patent for the purpose of identifying such nucleic acids for diagnosing a pathogenic infection, for example.

13. Claims 21-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 37-47 of copending Application No. 09/932,122. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are coextensive in scope. Claims 21-23 of the instant application are drawn to the same subject matter as claims 37-47 of the '122 application. Although each of claims 37-47 of the '122 application are not identical in scope to the claims of the instant application, the dependent claims of the '122 application specify the same chelators, chelator enhancing components, and concentration ranges of the instantly pending claims. Further, with regard to instantly pending claim 24, it would have been prima facie obvious to the ordinary artisan to improve hybridization between a primer and target or test nucleic acid during an amplification reaction for the purposes of improving the efficiency of the amplification reaction.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
9/20/2002